

## MOBILITY SPECTROMETER

[0001] This application claims priority to U.S. Provisional Application No. 60/193,659, filed Mar. 31, 2000, and to U.S. Provisional Application No. 60/185,781, filed Feb. 29, 2000.

[0002] The technology was developed with government support (NSF Reference No. CHE9629966). The government may have certain rights in the invention.

## FIELD OF THE INVENTION

[0003] The present invention relates generally to instrumentation and methodology for characterization of chemical samples based on improved ion mobility spectrometry (IMS) instrumentation. The improvements are also incorporated into a mobility-mass spectrometer, which is a tandem configuration of an ion mobility spectrometer (IMS) and a mass spectrometer (MS). This apparatus is an instrument for qualitative and/or quantitative chemical and biological analysis.

## BACKGROUND OF THE INVENTION

[0004] An ion mobility spectrometer is typically composed of an ionization source, a drift cell, and an ion detector, e.g. a sampling plate, an electron multiplier, or a mass spectrometer. Ion mobility spectrometry separates ions in terms of their mobility with reference to a drift/buffer gas measuring the equilibrium velocity which ions obtain. When gaseous ions in the presence of a drift gas experience a constant electric field, they accelerate until a collision occurs with a neutral molecule. This acceleration and collision sequence is repeated continuously. Over time, this scenario averages out over the macroscopic dimensions of the drift tube to a constant ion velocity based upon ion size, charge and drift gas pressure. The ratio of the velocity of a given ion to the magnitude of the electric field experienced by it is the ion mobility. In other words, the ion drift velocity ( $v_d$ ) is inversely proportional to the electric field strength (E) where the ion mobility  $K=v_d/E$  is a function of the ion volume/charge ratio. Thus IMS is a technique similar to mass spectrometry, having a separations component to it. IMS is generally characterized as having high sensitivity with moderate separation power. Separation efficiency is compromised when "bands" of the various ions spread apart as opposed to remaining together in a tight, well-defined plug. Thus, the quality of the electric field maintained in the drift cell is critical to preserving and perhaps improving separation efficiency; i.e., resolution.

[0005] Prior art instruments employ various methods to obtain a linear electric field including utilizing: 1) a series of equally spaced rings connected through a resistor chain, 2) a tube coated with a resistive material in U.S. Pat. No. 4,390,784 to Browning et al., or 3) by a more complex method such as a printed circuit board assembly drift tube in U.S. Pat. No. 6,051,832 and PCT WO 98/08087 to Bradshaw.

[0006] The combination of an ion mobility spectrometer (IMS) with a mass spectrometer (MS) has been known for a long time. In 1961 Barnes et al. were among the first to combine these two separation methods. Such instruments allow for separation and analysis of ions according to their mobility and their mass, which is often referred to as an two dimensional separation or two dimensional analysis. Young

et al. realized that a time-of-flight mass spectrometer (TOFMS) is the most preferred mass spectrometer type to be used in such a combination because its ability to detect simultaneously and very rapidly (e.g. with a high scan rate) all masses emerging from the mobility spectrometer. Their combination of a mobility spectrometer with a TOFMS, in the following referred to as a Mobility-TOFMS, is shown in FIG. 1. FIG. 1 illustrates means for ion generation (1), a mobility drift cell (2), a TOFMS (3), and a small orifice (24) for ion transmission from the mobility cell to the TOFMS in this prior art instrument.

[0007] Use of MS as a detector allows for resolution based on mass-to-charge ratio after separation based upon ion mobility. Other prior art instruments and methods using sequential IMS/MS analysis have been described (see, e.g., McKight, et al. *Phys. Rev.*, 1967, 164, 62; Young, et al., *J. Chem. Phys.*, 1970, 53, 4295; U.S. Pat. No. 5,905,258 of Clemmer et al.; PCT WO 00/08456 of Guevremont) but none combine the instrumental improvements disclosed presently. When coupled with the soft ionization techniques and the sensitivity improvements realizable through use of the drift cell systems herein disclosed, the IMS/MS systems and the corresponding analytical methods of the present invention offer analytical advantages over the prior art, particularly for the analysis of macromolecular species, such as biomolecules. Shoff and Harden pioneered the use of Mobility-MS in a mode similar to tandem mass spectrometry (MS/MS). In this mode, the mobility spectrometer is used to isolate a parent ion and the mass spectrometer is used for the analysis of fragment ions (also called daughter ions) which are produced by fragmentation of the parent ions. In the following this specific technique of operating a Mobility-MS is referred to as Mobility/MS, or as Mobility/TOF if the mass spectrometer is a TOFMS-type instrument.

[0008] The challenging issue when building a Mobility-MS is achieving a high ion transmission from the mobility region into the MS region of the tandem instrument. It is at this interface that the earlier goals of ion mobility technology of using a linear field appear incongruous with the goal of maximizing ion throughput across the IMS/MS interface. The mobility section is operating at a pressure of typically between 1 mTorr and 1000 Torr whereas the MS is typically operating at pressures below  $10^{-4}$  Torr. In order to maintain this differential pressure it is necessary to restrict the cross section of the opening that permits the ions to transfer from the mobility section to the MS section. Typically these opening cross section is well below  $1 \text{ mm}^2$ . Hence it is desirable to focus the ions into a narrow spatial distribution before this transmission occurs.

[0009] As discussed above, in the early development of IMS, it was believed that the use of focusing methods (i.e., non-linear fields) was detrimental because it was believed that such focusing methods would deteriorate the resolution of the mobility spectrometer. Also, many of the early mobility spectrometers were used to investigate the mobility constant of ions, in which case it is preferable to use a homogeneous field of known value along the ion drift path. Therefore, most instruments just used a large area ion detector at the end of the mobility drift and ion focusing was not an overarching concern. It was only when the need for compact and sensitive IMS emerged when the focusing of the drift ions was addressed.